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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,136	03/27/2001	Darrell C. Conklin	00-25	3811

7590 09/10/2002

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/819,136	CONKLIN ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --.

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,23,24 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3-5* is/are allowed.

6)☒ Claim(s) *1,2,6-8,23,24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 June 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-8, 23-24, 26 are pending.

Applicant's amendment of claims 7 and 8, in Paper No. 10, filed on 6/24/2002 acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

1. The use of the trademarks has been noted in this application. See, for example, "Qiagen", "Clonetech", etc. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Priority

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/193,642 filed on 3/31/2000.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on 6/24/2002 was filed after the mailing date of the first Office Action on the merits on 4/5/2002. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

4. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review. Applicant is required to submit the drawing corrections within the time period set in the attached Office communication. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDOMENT of the application. In addition, if amendments to the specification are needed due to drawing corrections, Applicant is requested to submit such amendments while the case is being prosecuted to expedite the processing of the application.

Claim Rejections - 35 USC § 112, Second Paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 8 is indefinite in the recitation of "wherein the at least 15 contiguous amino acids" as it is unclear if the claimed polypeptide comprises only 15 contiguous amino acid residues of SEQ ID NO: 2 or more than 15 contiguous amino acids of SEQ ID NO: 2. It is suggested that the term "at least" be deleted. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2, 6-7, 23-24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2 and polypeptides comprising the four disulfide core, follistatin, Kunitz or netrin proteinase inhibitor domains of the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for polypeptides comprising the immunoglobulin domain of the polypeptide of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

Claims 1, 2, 6-7, 23-24, and 26 are directed to a polypeptide comprising residues 203-286 of the polypeptide set forth in SEQ ID NO: 2. According to the specification, the polypeptide of SEQ ID NO: 2 encodes a multi-domain proteinase inhibitor. The polypeptide of SEQ ID NO: 2 comprises several domains which Applicants assert are those of different proteinase inhibitors (Table 1, page 9). In addition, the polypeptide of SEQ ID NO: 2 also comprises an immunoglobulin domain between residues 203-286. While Applicants have disclosed a function for the different proteinase inhibitor domains of the polypeptide of SEQ ID NO: 2, there is no disclosure in the specification of the specific function of the immunoglobulin domain of residues 203-286, such as its target or ligand or how it is related to the proteinase inhibitor function of the polypeptide which comprises it. In addition, the state of the art is silent as to the specific function or target of the immunoglobulin domain of the polypeptide of SEQ ID NO: 2. Therefore, due to the amount of information provided, and the state of the art in regard to the function/target of the immunoglobulin domain, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to determine the immunoglobulin domain's function and use. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

10. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

11. This rejection has been discussed at length in Paper No. 8, mailed on 4/5/2002.

12. Applicants argue that fusion proteins comprising the epitope (immunogenic fragment) and known immunogens are commonly used in the art to induce antibody production. Applicants also argue that the amendment made to claim 8 should overcome the instant rejection. In particular, Applicants argue that the claim now recites that the 15 contiguous amino acids are immunogenic, therefore arguments in regard to the function of a protein comprising at least 15 contiguous amino acid residues of SEQ ID NO: 2 are now moot.

13. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While it is agreed that to raise antibodies against specific epitopes, one can create a fusion protein wherein the epitope (immunogenic fragment) and a known immunogen are linked , the scope of the claim as written includes not only immunogenic fusion proteins but any protein of any function which comprises at least 15 contiguous amino acids of SEQ ID NO: 2 wherein the 15 contiguous amino acids comprise residues 117-122, 525-530, 283-288, or 50-55. The addition of the limitation "immunogenic" as it relates to the 15 amino acid residues does not define the specific function of a polypeptide comprising at least 15 amino acids of SEQ ID NO: 2 as encompassed by the claim, since any peptide can immunogenic. Therefore, as indicated in previous Office Action Paper No. 8, Applicants have not adequately described the genus of polypeptides claimed.

14. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any polypeptide comprising at least 15 contiguous amino acids of SEQ ID NO: 2 as

encompassed by the claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

15. This rejection has been discussed at length in previous Office Action Paper No. 8, mailed on 4/5/2002.

16. Applicants argue that fusion proteins comprising the epitope (immunogenic fragment) and known immunogens are commonly used in the art to induce antibody production. Applicants also argue that the amendment made to claim 8 should overcome the instant rejection. In particular, Applicants argue that the claim now recites that the 15 contiguous amino acids are immunogenic, therefore arguments in regard to the function of a protein comprising at least 15 contiguous amino acid residues of SEQ ID NO: 2 are now moot.

17. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. As indicated above, the scope of the claim includes any polypeptide which comprises at least 15 contiguous amino acids of SEQ ID NO: 2 as encompassed by the claim. Therefore, it is not clear how any polypeptide of any size which comprises at least 15 contiguous amino acids of SEQ ID NO: 2 as encompassed by the claim, can be used to raise antibodies against the 15 amino acid immunogenic fragment, since as known in the art, how the immunogenic fragment is presented to the immune system will determine if antibodies will be made. If, for example, the polypeptide is much larger that the immunogenic fragment, it can fold in such a way that the immunogenic fragment is no longer "seen" by the immune system. Under those circumstances, such polypeptide cannot be used to raise antibodies to that specific immunogenic fragment. In addition, enablement arguments presented in previous Office Action

Paper No. 8 in regard to determining the function of the polypeptides claimed would still apply since the scope of the claim has not changed due to the amendment presented. Therefore, Applicants have not presented sufficient guidance to enable one of skill in the art to make and practice the invention as claimed.

Allowable Subject Matter

18. Claims 3-5 appear to be allowable over the prior art of record.

Conclusion

19. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

20. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
August 29, 2002

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600